NDA 17-488/S-101, S-104
NDA 17-489/S-084, S-087
NDA 17-735/S-083, S-087
NDA 18-354/S-034, S-037
NDA 17-919/S-065, S-069
NDA 18-985/S-029, S-030, S-033

AUG 27 1999

The R. W. Johnson Pharmaceutical Research Institute
Attention: Ms. Donna Panasewicz
Manager, Regulatory Affairs
Route 202, P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Panasewicz:

Please refer to your supplemental new drug applications dated May 22, 1997, received May 23, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for: Ortho-Novum 1/35 21 Tablets (NDA 17-489); Modicon 21 (NDA 17-488): Modicon 28 (NDA 17-735): Ortho-Novum 1/35 28 Tablets (NDA 17-919); Ortho-Novum 7/7/7 (NDA 18-985); and Ortho-Novum 10/11 (NDA 18-354).

We acknowledge receipt of your submissions dated July 10, 1997, July 28, 1997 and November 10, 1998, that reference the multiple NDA's listed above.

These supplemental new drug applications provide for:

1. **INDICATION AND USAGE** section:

   Table 1 has been updated.

2. **WARNING** section:
   The second paragraph of the **Carcinoma of the Reproductive Organs and Breast** subsection was revised to read:

   "A meta-analysis of 54 studies reports that women who are currently using combined oral contraceptives or have used them in the past 10 years are at slightly increased risk of having breast cancer diagnosed although the additional cancers tend to be localized to the breast. There is no evidence of an increased risk of having breast cancer diagnosed 10 or more years after cessation of use.

   In addition, in the first sentence of the last paragraph, the word **"intraepithelial"** has been added to the description of cervical neoplasia.

3. **PRECAUTION** Section, **Nursing Mother** subsection: Second and third sentence, the word "combination" has been added so that the sentences now read:

"... In addition, combination oral contraceptives given in the postpartrum period may interfere with lactation by decreasing the quantity and quality of breast milk. If possible, the nursing mother should be advised not to use combination oral contraceptives but to use..."

4. **PEDIATRIC USE** section has be added to read:

"Safety and efficacy of ORTHO-NOVUM Tablets and MODICON Tablets has been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 16 and for users 16 years and older. Use of this product before menarche is not indicated."

5. **WARNING** section, **Hepatic Neoplasia**, the second paragraph has been modified to read:

"Studies have shown an increased risk of developing hepatocellular carcinoma in oral contraceptive users. However, these cancers are rare in the U.S.",

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the submitted final printed labeling (package insert submitted November 10, 1998, patient package insert submitted November 10, 1998). Accordingly, these supplemental applications are approved effective on the date of this letter.

In addition, please submit three copies of the introductory promotional materials that you propose to use for these products. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you sLibmit a copy of the letter to this NDA and a copy to the following address:

MED WATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Jennifer Mercier, Project Manager, at (301) 827-4260. Sincerely,

Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation Ill
Center for Drug Evaluation and Research